REMARKS

Claims 28, 30, 31 and 33-36 have been amended. Claims 39 and 40 have been added. No new matter has been added. Claim 38 has been canceled. Claims 1-27 were previously canceled. Claims 28-40 are currently pending in this application.

Obviousness Type Double Patenting

As the claims of the present specification are subject to further change, Applicant respectfully requests that this rejection be held in abayance until the claims are otherwise in a condition for allowance.

35 U.S.C. §112, Second Paragraph

Claim 34 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The examiner states that the term "GP88" is not clearly defined since abbreviations often have more than one meaning. Claim 34 has been amended to include the term "PC Cell Derived Growth Factor" in place of GP88.

35 U.S.C. § 112, First Paragraph: Enablement

Claims 28-38 stand rejected under 35 U.S.C. § 112, first paragraph. The examiner notes that the specification is enabling for a method of inhibiting the growth of a tumor cell and method of inhibiting the protein expression of PCDGF in a cell by the subcutaneous injection of PCDGF antisense targeted to SEQ ID NO:16 using primer pairs SEQ ID NO:12 and SEQ ID NO:14. The examiner, however, states that the specification does not reasonably enable the present claims. This rejection is respectfully traversed.

The Office Action maintains the enablement rejection for the same reasons as stated in the February 3, 2006 Office Action. The present Office Action sets forth additional reasoning to support the rejection. Applicant also incorporates the remarks contained in the Amendment filed on June 5, 2006 and provides the additional remarks below.

The Examiner alleges that it would require undue experimentation to determine which cells to target with PCDGF antisense oligonucleotides. Applicant respectfully disagrees. Some or even a considerable amount experimentation is permissible, if it is routine or if the specification provides guidance as to the direction in which the experimentation should proceed. Ex parte Jackson, 217 U.S.P.Q. 804 (Bd.App.1982). In view of the guidance in the specification, presence of working examples, the state of prior art, relative skill of those in the art, and the breadth of the claims, undue experimentation would not be required to practice the claimed invention. M.P.E.P. §2164.06.

Initially, the Office Action states that it would require undue experimentation to determine which cells to target. Applicant submits that in view of the scope of the claims, the direction provided in the specification and the level of skill in the art, undue experimentation would not be required to determine which cells to target since the specification and claims specifically provide this information. The claims are directed to administering PCDGF antisense oligonucleotides to a tumor cell and inhibiting the expression of PC Cell Derived Growth Factor protein in a cell. Thus, the claims themselves recite that tumor cells and cells expressing PC Cell Derived Growth Factor protein are the cells to be targeted by the antisense oligonucleotides. Those of ordinary skill in the art are readily able to identify tumor cells by a variety of methods. For example, the Specification provides guidance for detecting tumor cells and cells that

express PC Cell Derived Growth Factor protein. Specification at [0097]-[0104]. The Specification notes that disclosed antibodies and antibody fragments can be used to detect cells expressing PC Cell Derived Growth Factor protein by immunofluorescence techniques and immunoassay techniques. Id. Such techniques are readily performed by those skilled in the art. Moreover, the Specification provides examples of detecting the expression of PC Cell Derived Growth Factor protein. See Specification at [0146]-[0152]. Thus, one of skill in the art can readily identify target cells by a variety of methods disclosed in the Specification.

The Office Action further states that the present invention is not enabled because it would require undue experimentation to determine routes of administration other than by injection; dosages; disposition of the antisense oligonucleotides in cells; the half-life of the oligonucleotide molecule in vivo; and the stability of the oligonucleotide in vivo. Office Action at 9. Taken together, the PTO appears to require the Applicant to conduct clinical trials in order to enable the claimed invention. It is well established that clinical testing is not required to establish that an invention is enabled. In re Brana, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995)(stating that requiring in vivo human testing to show effectiveness and safety of a drug "confuses the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption."). Applicants need not have produced or perfected a marketable product in order to have enabled the present claims. Rather, the Applicant has provided ample working examples in a well-accepted animal model demonstrating the administration of antisense molecules in vivo and the resulting inhibition of tumor cell growth as evidenced by tumor shrinkage. Determining particular dosages, routes of administration, and stability is a matter of routine experimentation and incidental to the claimed invention.

The rejection appears to be incorrectly based on generalized statements regarding antisense technology that are not related to the claimed invention. For example, the Examiner states that Agrawal et al. establish that the "feasibility of antisense therapy for one antisense does not demonstrate the feasibility for a wholly different antisense oligonucleotide." Office Action at 9. Agrawal et al., however state that antisense oligonucleotide therapeutics can be as simple as complementary base recognition if proper design precautions and controls are used. Agrawal et al. at 80. Applicant's successful application of these principles demonstrates that Agrawal et al. are correct. Further, Applicant's invention is not directed to antisense generally. Rather, the claims are directed to PCDGF antisense oligonucleotides. As discussed in the Amendment filed on June 5, 2006, the articles cited by the Examiner show that antisense is a viable technology, particularly where a target for the antisense is identified, as is the case here.

Independent claim 28 is directed to inhibiting the growth of a tumor cell in a mammal comprising administering a PC Cell Derived Growth Factor antisense oligonucleotide to the tumor cell by injection. Independent claims 31 and 35 are directed to administering a PCDGF antisense oligonucleotide to a tumor cell to reduce tumor size and reduce the proliferation of the tumor cell, respectively. Independent claim 34 is directed to administering a PCDGF antisense oligonucleotide to a cell expressing PC Cell Derived Growth Factor protein to inhibit expression of the PC Cell Derived Growth Factor protein. The claims recite that the antisense oligonucleotide is an oligonucleotide targeted to at least a portion of SEQ ID NO:16. In view of the guidance in the specification, the presence of working examples, the state of prior art, the relative skill of those in the art and the breadth of the claims, it would not require undue experimentation to practice the claimed invention.

The present claims recite administering a PCDGF antisense oligonucleotide. Applicant provides specific examples of the invention. See Specification at [0167]-[0190]. Moreover, Applicant provides additional guidance in the Specification that would enable one skilled in the art at the time the invention was made to make and use the invention without undue experimentation.

For example, Applicant provides a target sequence (e.g., SEQ ID NO:16) for the antisense oligonucleotides. The Examiner also notes that various other sequences for PC Cell Derived Growth Factor protein were known by those skilled in the art. Office Action at 10-11. Those of ordinary skill in the art would readily appreciate that a PCDGF antisense oligonucleotide is an oligonucleotide that is complimentary to a DNA or RNA sequence for PC Cell Derived Growth Factor protein. As complimentarity is well understood, those of ordinary skill in the art would readily be able to determine potential antisense oligonucleotides. The Specification also provides guidance for determining suitable PCDGF antisense oligonucleotides. The Specification states that an exemplary antisense oligonucleotide is preferably between 15-30 or 18-30 nucleotides in length and is hybridizable to the coding sequence, 3′ or 5′ untranslated regions, intronic sequences or to mRNA. Specification at [0113]-[0116]. The Specification notes that sequences around the initiation site provide efficient antisense activity and provides examples of specific antisense sequences. Specification at [0190].

Furthermore, the Specification provides ample guidance for a variety of effective delivery methods. Specifically, the Specification notes that the preferred PCDGF antisense oligonucleotides are "those oligonucleotides which are stable, have a high resilience to nucleases (enzymes that could potentially degrade oligonucleotides), possess suitable pharmacokinetics to allow them to traffic to disease tissue at non-toxic doses, and have the ability to cross through plasma membranes." Specification at

paragraph [0117]. The Specification notes that phosphorothioate antisense oligonucleotides, peptide nucleic acids, and other stabilized forms of oligonucleotides are effective for delivery and that delivery mediated by cationic liposomes, by retroviral vectors and direct delivery are efficient. Specification at paragraphs [0118] and [0119] (citations omitted). As indicated in Wang et al., systemic and local delivery of phosphorothioate antisense oligonucleotides, was known to be effective at the time the application was filed.

Applicant has demonstrated the roll of PCDGF in tumorigenicity and has also shown that suppression of PCDGF reduces tumorigenicity, tumor size, and the proliferation of tumor cells. Specification at [0072]-[0082]. Moreover, Applicant has shown, in vivo, that antisense achieved these results. Specification at [0167]-[0190].

Applicant provides additional guidance to one of skill in the art. For example, the Specification teaches how to judge the efficiency of a sequence to inhibit PC Cell Derived Growth Factor protein expression and various dosages for providing antisense oligonucleotides to a cell type of interest. Specification at [0190]. In order to determine efficiency, the Specification teaches collecting of cell samples at various intervals and measuring the level of PC Cell Derived Growth Factor protein expression (e.g., by Western blot analysis or EIA techniques, which are known). Id.

Thus, any necessary experimentation conducted by one of ordinary skill in the art would not be undue. Such experimentation would be routine and/or well guided by the present Specification. Therefore, one of ordinary skill in the art would have been able to practice the invention as recited by the present claims at the time this application was filed. For at least these reasons, this rejection under 35 U.S.C. § 112, First Paragraph should be withdrawn.

35 U.S.C. § 112, First Paragraph: Written Description

Claims 28-37 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner states that because the claims do not recite a sequence identifier relating to PC Cell Derived Growth Factor protein, the sequence is defined by its function. The Examiner states, therefore, that the claims embrace antisense oligonucleotides that inhibit the expression of PC Cell Derived Growth Factor protein or any molecule with analogous activity to that of PC Cell Derived Growth Factor protein, along with any isoform or allele, variant, polymorphic or otherwise that is similar to these families of proteins and retains the same activity as PC Cell Derived Growth Factor protein.

Independent claims 28, claims 28, 31, 34 and 35 have been amended to recite that the oligonucleotide is an oligonucleotide targeted to at least a portion of SEQ ID NO:16. Accordingly, the Specification would have conveyed to one of skill in the art at the time the application was filed that Applicant had possession of the claimed invention. Therefore, Applicant respectfully requests withdrawal of this rejection.

35 U.S.C. § 112, First Paragraph: New Matter

Claims 30, 33 and 36 stand rejected under 35 U.S.C. § 112, first paragraph, for containing new matter. Regarding claims 30 and 33, the Examiner states that the phrase "at least about 15 nucleotides" is new matter. Claims 30 and 33 have been amended to recite "about 15-30 nucleotides." Support for this amendment is found in paragraph [0190] of the Specification. The Examiner states that the phrase "at least about 80 percent" in claim 36 is new matter. As recommended by the Examiner, claim 36 has been amended to recite "wherein the proliferation of the tumor cell is inhibited by 80 percent."

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. If the Examiner should believe that anything further may be required to place this application in even better form for allowance, she is cordially invited to telephone the undersigned attorneys for Applicant.

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Respectfully submitted,

By _____

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